



Burning Mouth Syndrome – Known and Unknown

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Abstract

The aim of this literature review was to provide a brief perspective over the scientific research of the condition known as burning mouth syndrome. Information from review articles, original studies, and dissertations was gathered using keywords describing etiological factors, clinical, laboratory findings and treatment protocols. We compiled information on potential etiological factors, symptoms, and potential treatments from the fifty-three included studies on dental and general health issues in patients complaining of burning sensations in their mouths. Despite the numerous attempts by dental and medical professionals to diagnose and treat mouth burning, the etiology and pathogenesis of this disorder remain rather unclear. In most cases, it is concluded that further research is needed with the inclusion of more patients, administering a long-term therapy, and monitoring the results.

Keywords

glossodynia, stomatodynia, stomatopyrosis

INTRODUCTION

One group of patients who present difficulties for diagnosis and future treatment can be identified among those seeking dental care. The medical history of such patients is remarkable for burning, pain, and change in the taste with different intensity, duration, and periods of exacerbation. A prerequisite for the diagnosis of burning mouth syndrome (BMS) is the absence of radiographic findings and of clinically observed pathological changes in the soft and hard tissues in the oral cavity.^[1]

Considering such a condition includes a great number of clinical and laboratory tests. It is necessary to assess the general health and dental status and, finally, the mental status of patients with such complaints. The literature examining this issue addresses the influence of local factors in the oral cavity such as fungal or bacterial infections, a trau-

matic effect of prosthetic restorations, allergic reactions to dental materials, increased corrosion potential, and para-functional habits. After eliminating these possible causes, if no improvement occurs, the general health status should be assessed based on blood count and laboratory parameters indicative of vitamin deficiencies and liver, pancreas, kidneys, thyroid gland, and digestive system functioning. Very often, such extensive testing may not lead to a definitive diagnosis. In such cases, psychological aspects are considered cofactors methods for confirming anxiety or depression and measuring stress levels should be used. It is possible to make this assessment by psychometric tests or by measuring the levels of stress hormones secreted by the adrenal glands.

Epidemiological studies report prevalence rates varying from 2.7% to 35% among the study groups. These differences can be explained by the ambiguity in the diagnostic

criteria, which, in turn, makes it difficult to define a treatment protocol.

Definition

Burning mouth syndrome is a condition for which it is difficult to establish standardized diagnostic criteria and confirm exact etiology.^[2-5] Also, attempts to provide a precise definition are numerous. The American Academy of Oro-facial Pain describes it as a burning sensation in the oral cavity despite the absence of clinical findings in the mucosa or laboratory abnormalities.

The International Headache Society^[6,7] has set out the following main criteria for such a diagnosis:

- 1) intraoral burning sensation recurring daily and lasting for most of the day
- 2) no changes in the oral mucosa
- 3) no systemic diseases.^[8,9]

The scientific literature abounds with synonyms for this term, which adds to clinicians' confusion and uncertainty. Stomatodynia, stomatopyrosis, glossodynia, glossopyrosis, and subprosthetic stomatitis are only some of the terms used synonymously for this condition.^[10] Recapitulating all of the efforts toward a definition, it is clear that the various researchers agree on the idea of primarily subjective complaints with no observable intraoral changes.^[11]

Epidemiology

The epidemiological incidence rate of this syndrome can only be generalized based on the findings of larger studies in individual countries. In Sweden, Bergdahl et al. found 53 individuals (3.71%) out of a cohort of 1,427 patients to have BMS.^[12] Dibello et al. found that BMS symptoms were present in 35% of 120 patients.^[13] The incidence rate of such complaints among the American population was reported to be 2.7%.^[14] The differences in these rates can be attributed to the lack of universally accepted clinical criteria, the use of various diagnostic methods, and the heterogeneity of the methods in the cited studies.^[2] All studies present different epidemiological data but conclude that BMS is more prevalent in postmenopausal females and that the incidence of such complaints rises with age in both sexes.^[15,16]

Classification

Burning mouth syndrome is generally classified into two types: primary and secondary. In the primary form of this condition, no causative factors can be found.^[17] Secondary BMS patients are those whose treatment of a local systemic or psychological underlying disease results in relief or resolution of their oral complaints.^[18] According to the symptom intensity over 24 hours, 3 subgroups of patients can be differentiated. The first subgroup includes patients who experience burning sensation every day, which is not present when waking up, becomes more intense during the

day, and is most intense in the evening; the causes here are mainly systemic disease or vitamin deficiencies. The second subgroup also includes patients with daily complaints, but their complaints persist all day long, from waking up, and even making it difficult to fall asleep at night; in such cases, psychological problems should be considered. The third subgroup includes patients who have asymptomatic days; often the cause of this condition in such cases is an allergic reaction.^[3,13,14,19]

Etiology

The etiological factors in secondary BMS are too numerous to list and can be divided into three main groups – general, local, and psychological.^[20-22]

Among the common etiological factors, micronutrient deficiencies are often considered: (Fe, Zn), B-complex vitamins. Attempts to administer drug replacement therapy did not lead to statistically significant results and effects on the symptoms among the patients in experimental and control groups.^[14,15,17,23]

Elevated blood glucose levels can be a cause of subjective symptoms in the oral cavity. In patients suffering from impaired carbohydrate metabolism over a long period of time, degenerative changes in sensory nerve fibers are possible. A logistic regression model demonstrates the development of diabetic polyneuropathy as a significant factor in patients with BMS.^[24]

Femiano et al. reported that changes in the structure and function of the thyroid gland were found in 69% of a group of patients with burning in the oral cavity. The pathological change in the thyroid gland is more often in the direction of hypothyroidism; oral complaints improve with the administration of hormone therapy. The authors suggest an influence on the maturation and specialization of taste receptors.^[25] Higher prevalence of thyroglobulin and thyroid microsomal antibodies were found in the sera of BMS patient compared to healthy control groups.^[18]

Autoimmune parietal cells antibodies were also present in blood tests of BMS individuals. Damage to the intestinal mucosa reduces vitamin B12 absorption and causes pernicious anemia, but injectable vitamin B12 administration has not always been effective.^[26]

Regarding endocrine changes, it is important to consider the role of estrogens and androgens as an etiological factor in BMS.^[27] Receptors for female sex hormones have been found in the oral mucosa, the salivary glands, and the trigeminal nerve. Decreased amounts of sex hormones and their precursors result in changes in the reactivity and expression of neurons in various parts of the nervous system.^[3] Estrogen upregulates the expression of nociceptive receptors on the nerve cells, the larger number of pain receptors generates electrical impulses which brain perceives as pain. In contrast to these findings, research shows that estrogen reduces pain by suppressing nerve growth factors.^[28]

Another topic of research has been the composition of saliva in BMS patients. Levels of IgE antibodies, interleu-

kins, nerve growth factors, soluble CD14 proteins, and toll-like receptors showed controversial results, and the final conclusion was that the information is still preliminary, and no salivary tests were confirmed as definitely diagnostic.^[29-31]

In scientific literature, increased levels of mental stress and anxiety are often considered conditions related to BMS. In such conditions, many endocrine and metabolic changes occur, among which, a change in the cortisol secretion. As a major glucocorticoid hormone, cortisol has a stable and reproducible rhythm of secretion under constant physiological conditions.^[32,33] The lowest cortisol level is observed at midnight. In the hours between 02.00 a.m. and 03.00 a.m., there is an increase, which reaches its peak around 08.30 a.m., followed by a drop to the lowest level and a subsequent increase, thus maintaining a 24-hour circadian rhythm. The peak blood level is approximately 399 nmol/L and the trough level is <50 nmol/L.^[32,34] Undoubtedly, it participates in the metabolism of fats, carbohydrates, proteins, and minerals. It maintains the reactivity of blood vessels and the nervous system and models the response to stressful situations.^[8,35,36] Dibello et al. discussed the results in connection with assessed high levels of stress and depression.^[13] A positive correlation between the severity of oral symptoms and the severity of psychogenic factors was demonstrated, and patients suffering from burning mouth syndrome were more often nervous and had impaired quality of life.^[37] The pathophysiological mechanism of this correlation can be explained by a change in the cortisol metabolism.^[7,8] Emotional stress can also lead to the development of parafunctional habits such as bruxism or incorrect positioning of the tongue, which can result in pain or burning sensation.^[10]

The modern approach to explore the pathogenic mechanism of this condition has been increasingly involving a precise assessment not only of the mental status but also of the structure of the peripheral and central nervous system.^[38] Researchers used laser stimulation of the tongue mucosa and concluded that 50% of the patients had changes in the peripheral trigeminal nerves. Decreased perception of thermal stimuli and increased pain sensitivity were reported.^[4] Yilmaz et al. performed histological examinations of the tongue epithelium of patients with BMS, the results demonstrating significant loss of nerve fibers.^[39] Systemic analysis of the trigeminal nerve reflexes showed lesions in the ganglia nuclei located in the brainstem.^[16] Electric taste and tingling test demonstrate results of elevated thresholds that could be explained with hypofunction of chorda tympani.^[40]

Positron emission tomography images show changes in dopamine metabolism of nigrostriatal neurons. Interpretation of this information leads to the conclusion that in some patients, changes similar to those in Parkinson's disease are found.^[41]

In articles by authors who are dental specialists, attention is paid to local factors in the oral cavity that could cause a burning sensation. Fungal infections are common in pa-

tients with complaints of burning, but cases of coliforms and fusobacteria were also reported.^[4,42] The presence of sharp edges, inaccuracies, corrosion changes in prosthetic restorations and fillings leads to a chronic injury of the oral mucosa and the occurrence of painful symptoms, growing into a burning sensation.^[43] Apart from the mechanical influence of the dental restorations, sensitization to the ingredients of which they are made should not be ruled out. It is debatable whether allergic contact stomatitis may present with symptoms of intraoral burning.^[2,3,44-46] In her dissertation, Ivanova also concluded that burning sensation without any evident mucosal changes is not related to hypersensitivity reactions to restorative materials.^[47] Examining the role and participation of local etiological factors in the development of burning symptoms, other authors found that sensitization to dental materials should not be overlooked.^[48,49]

Treatment

The therapeutic approach in patients suffering from BMS always includes psychological support and reassurance that the complaints are not a sign of a life-threatening condition. Patients with BMS should also be informed that treatment is a long-term process and that full symptom resolution is not always achieved.^[18,44,50]

In cases of a burning sensation in the oral cavity, in which deficiencies of vitamins and micronutrients have been found, management of symptoms should start with replacement therapy. The duration of the administration of food supplements and the final results vary considerably in different cases. According to Cho et al., 30% of patients with vitamin B1, B2, and B6 deficiencies showed improvement after receiving these vitamins for four weeks.^[15] Alpha-lipoic acid also has many beneficial effects on the nervous system and for that reason, many researchers tried to include it in the treatment of BMS. This is a "first-class" agent, according to some authors, and administering it has important effects.^[51] Other studies showed that the success rate with placebo administration was the same as with lipoic acid.^[17] There has been a large number of attempts to administer topical agents such as fruit juices, decoctions of herbs, hot peppers, non-steroidal anti-inflammatory drugs, artificial sweeteners, agents for the treatment of mucosal lesions, and fungal infections. None of the listed suggestions can be conclusively backed by results that are unanimous.^[3,17,52]

Femiano et al. discussed drug correction of low thyroid hormone levels and its effect on the burning sensation in the oral cavity. In patients with changes in the parenchyma of the gland, relief of symptoms was achieved after taking thyroxine in doses consistent with the severity of hypothyroidism.^[25]

High doses of melatonin administration did not improve patients state even such treatment had diverse side effect which resulted in discontinuation.^[53]

Patients in whom the main cause of complaints was their mental status were treated with anxiolytics, antidepress-

sants, antiepileptics, antihistamines, and benzodiazepines. In these cases, in the discussion, the results were also compared with those in the placebo groups and no significant difference could be confirmed. There is a concern that the adverse effects of these medications, such as dry mouth, drowsiness, and cardiac complications, are more common and outweigh the control of the burning mouth sensation. For that reason, the authors limit their recommendations for the use of such drugs in the treatment of BMS.^[4,39,42]

CONCLUSION

Despite the numerous attempts by dental and medical professionals to diagnose and treat mouth burning, the etiology and pathogenesis remain rather unclear. In most cases, it is concluded that further research is needed with the inclusion of more patients, administering a long-term therapy, and monitoring the results. Considering only one etiological factor in no way leads to a positive change and an optimistic prognosis. There are no clear criteria for diagnosing burning mouth syndrome and it cannot be stated with certainty whether it is a syndrome or a symptom. The result is an inconsistency in the diagnostic protocol and hence inadequate treatment. Relative therapeutic success can be achieved with a strict individual approach to each case and, certainly, medical professionals should provide psychological support and should model the patient's behavior and his/her perception of this problem.

Conflict of interest statement

The authors declare no conflict of interest.

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Синдром горящего рта – известный и неизвестный. Обзор литературы.

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Резюме

Целью данного обзора литературы является представление краткого обзора научных исследований состояния, известного как синдром горящего рта. Информация из обзорных статей, оригинальных исследований и диссертаций была собрана с использованием ключевых слов, описывающих этиологические факторы, клинические, лабораторные данные и протоколы лечения. Мы собрали информацию о потенциальных этиологических факторах, симптомах и потенциальных методах лечения из пятидесяти трёх включенных исследований стоматологических и общих проблем со здоровьем у пациентов, жалующихся на жжение во рту. Несмотря на многочисленные попытки стоматологов и врачей диагностировать и лечить жжение во рту, этиология и патогенез этого расстройства остаются довольно неясными. В большинстве случаев делается вывод о необходимости дальнейших исследований с включением большего количества пациентов, назначением долгосрочной терапии и мониторингом результатов.

Ключевые слова

глоссодиния, стоматодиния, стоматопиروز
